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## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: \_\_\_\_\_ Examiner #: \_\_\_\_\_ Date: \_\_\_\_\_  
Art Unit: \_\_\_\_\_ Phone Number 30 \_\_\_\_\_ Serial Number: \_\_\_\_\_  
Mail Box and Bldg/Room Location: \_\_\_\_\_ Results Format Preferred (circle): PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: \_\_\_\_\_

Inventors (please provide full names): \_\_\_\_\_

Earliest Priority Filing Date: \_\_\_\_\_

*\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Ján Delaval  
Reference Librarian  
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jan.delaval@uspto.gov

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Searcher: <u>Oh</u>	NA Sequence (#) _____	STN _____
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Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: <u>3/15/83</u>	Bibliographic _____	Dr. Link _____
Date Completed: <u>3/15/83</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems <u>✓</u>
Clerical Prep Time: <u>15</u>	Patent Family _____	WWW/Internet _____
Online Time: <u>+10</u>	Other _____	Other (specify) _____

egin 5,73,155,399

03may03 07:31:33 User208760 Session D2298.2

\$0.00 0.071 DialUnits File410

\$0.00 Estimated cost File410

\$0.03 TELNET

\$0.03 Estimated cost this search

\$0.35 Estimated total session cost 0.161 DialUnits

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File 5:Biosis Previews(R) 1969-2003/Apr W4

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\*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 73:EMBASE 1974-2003/Apr W4

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\*File 73: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 155:MEDLINE(R) 1966-2003/Apr W4

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\*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.

File 399:CA SEARCH(R) 1967-2003/UD=13818

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\*File 399: Use is subject to the terms of your user/customer agreement.

Alert feature enhanced for multiple files, etc. See HELP ALERT.

Set Items Description

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? s (cd40L or cd40(w)ligand) and (treat? or therap? or prevent? or suppress? or block? or inhibit?) (20n) (cancer? or tumor? or tumour?)

Processing

Processing

Processing

Processing

Processing

Processing

	4407	CD40L
	17518	CD40
	342860	LIGAND
	7980	CD40(W)LIGAND
	6000244	TREAT?
	5560564	THERAP?
	1926273	PREVENT?
	746765	SUPPRESS?
	1172882	BLOCK?
	3709658	INHIBIT?
	1990055	CANCER?
	2021890	TUMOR?
	268769	TUMOUR?
	1025598	(((((TREAT? OR THERAP?) OR PREVENT?) OR SUPPRESS?) OR BLOCK?) OR INHIBIT?) (20N) ((CANCER? OR TUMOR?) OR TUMOUR?) (CD40L OR CD40(W)LIGAND) AND (TREAT? OR THERAP? OR PREVENT? OR SUPPRESS? OR BLOCK? OR INHIBIT?) (20N) (CANCER? OR TUMOR? OR TUMOUR?))
S1	745	

? s s1 and photodynamic

	745	S1
	26253	PHOTODYNAMIC
S2	1	S1 AND PHOTODYNAMIC

? t s2/3/all

2/3/1 (Item 1 from file: 399)

DIALOG(R) File 399:CA SEARCH(R)

(c) 2003 American Chemical Society. All rts. reserv.

135339226 CA: 135(24)339226q PATENT

Method for treatment of tumors using photodynamic therapy

INVENTOR(AUTHOR): Fanslow, William C., III; Thomas, Elaine K.

LOCATION: USA

ASSIGNEE: Immunex Corporation

PATENT: PCT International ; WO 200180888 A2 DATE: 20011101

APPLICATION: WO 2001US13616 (20010425) \*US PV199545 (20000425)

PAGES: 24 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

? s s1 and cd30?

745 S1

5966 CD30?

S3 33 S1 AND CD30?

? rd s3

...completed examining records

S4 25 RD S3 (unique items)

? t s4/3/all

4/3/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

13501169 BIOSIS NO.: 200200129990

Depletion of normal B-lymphocytes by rituximab therapy alters serum cytokine levels, resolves B-symptoms and induces clinical remissions in patients with relapsed classical Hodgkin's disease (HD).

AUTHOR: Younes Anas(a); Romaguera Jorge(a); Hagemeister Frederick(a); McLaughlin Peter(a); Rodriguez Maria Alma(a); Fiumara Paolo(a); Goy Andre(a); Jeha Sima; Manning John; Medeiros L Jeffrey; Martinez Rudy F(a); Cabanillas Fernando(a)

AUTHOR ADDRESS: (a)Lymphoma/Myeloma, M.D.Anderson Cancer Center (MDACC), Houston, TX\*\*USA

JOURNAL: Blood 98 (11 Part 1):p132a November 16, 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001

ISSN: 0006-4971

RECORD TYPE: Abstract

LANGUAGE: English

4/3/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.

13112983 BIOSIS NO.: 200100320132

A pilot study of rituximab in patients with relapsed Hodgkin's disease of classical type.

AUTHOR: Younes A(a); Romaguera J(a); Hagemeister F(a); Rodriguez M(a); McLaughlin P(a); Medeiros J(a); Cabanillas F(a)

AUTHOR ADDRESS: (a)U.T. M.D. Anderson Cancer Center, Houston, TX\*\*USA

JOURNAL: Blood 96 (11 Part 1):p733a November 16, 2000

MEDIUM: print

CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000

SPONSOR: American Society of Hematology

ISSN: 0006-4971

RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

4/3/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

13057538 BIOSIS NO.: 200100264687  
Chronic lymphocytic leukemia B cells impair immunoglobulin class switching  
by inducing CD30+ suppressor T cells.  
AUTHOR: Cerutti Andrea(a); Kim Edmund C(a); Zan Hong(a); Schaffer Andras(a)  
; Casali Paolo(a)  
AUTHOR ADDRESS: (a)Weill Medical College of Cornell University, 1300 York  
Avenue, New York, NY, 10021\*\*USA  
JOURNAL: FASEB Journal 15 (5):pA1202 March 8, 2001  
MEDIUM: print  
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies  
for Experimental Biology on Experimental Biology 2001 Orlando, Florida,  
USA March 31-April 04, 2001  
ISSN: 0892-6638  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

4/3/4 (Item 4 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

13033028 BIOSIS NO.: 200100240177  
Thiols decrease cytokine levels and down-regulate the expression of  
CD30 on human allergen-specific T helper (Th) 0 and Th2 cells.  
AUTHOR: Bengtsson A(a); Lundberg M; Avila-Carino J; Jacobsson G; Holmgren A  
; Scheynius A  
AUTHOR ADDRESS: (a)Department of Medicine, Unit of Clinical Allergy  
Research, Karolinska Hospital L2: 04, 171 76, Stockholm:  
asa.bengtsson@mb.ks.se\*\*Sweden  
JOURNAL: Clinical and Experimental Immunology 123 (3):p350-360 March, 2001  
MEDIUM: print  
ISSN: 0009-9104  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

4/3/5 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12615531 BIOSIS NO.: 200000369033  
TTRAP, a novel protein that associates with CD40, tumor necrosis  
factor (TNF) receptor-75 and TNF receptor-associated factors (TRAFs), and  
that inhibits nuclear factor-kappaB activation.  
AUTHOR: Pype Stefan; Declercq Wim; Ibrahimi Abdelilah; Michiels Christine;  
Van Rietschoten Johanna G I; Dewulf Nathalie; de Boer Mark; Vandenabeele  
Peter; Huylebroeck Danny(a); Remacle Jacques E  
AUTHOR ADDRESS: (a)Department of Cell Growth, Differentiation and  
Development, Flanders Interuniversity Institute for Biotechnology,  
University of Leuven, Herestraat 49, Campus Gasthuisberg, B-3000, Leuven  
\*\*Belgium  
JOURNAL: Journal of Biological Chemistry 275 (24):p18586-18593 June 16,

2000  
MEDIUM: print  
ISSN: 0021-9258  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

4/3/6 (Item 6 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

11525042 BIOSIS NO.: 199800306374  
Enhancement of antitumor immunity by expression of CD70 (CD27 ligand) or CD154 (**CD40 ligand**) costimulatory molecules in tumor cells.  
AUTHOR: Couderc Bettina; Zitvogel Laurence; Douin-Echinard Victorine; Djennane Leila; Tahara Hideaki; Favre Gilles; Lotze Michael T; Robbins Paul D(a)  
AUTHOR ADDRESS: (a)Dep. Mol. Genet. and Biochem., W1246 Biomed. Sci. Tower, Univ. Pittsburgh Sch. Med., Pittsburgh,\*\*USA  
JOURNAL: Cancer Gene Therapy 5 (3):p163-175 May-June, 1998  
ISSN: 0929-1903  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

4/3/7 (Item 7 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
(c) 2003 BIOSIS. All rts. reserv.

11226541 BIOSIS NO.: 199800007873  
**CD30** ligand in lymphoma patients with **CD30**!+ tumors.  
AUTHOR: Younes Anas(a); Consoli Ugo; Snell Virginia; Clodi Katharina; Kliche Kay-Oliver; Palmer J Lynn; Gruss Hans J; Armitage Richard; Thomas Elaine K; Cabanillas Fernando; Andreeff Michael  
AUTHOR ADDRESS: (a)Dep. Hematol., Section Lymphoma, Univ. Texas M.D. Anderson Cancer Cent., 1515 Holcombe Blvd., Ho\*\*USA  
JOURNAL: Journal of Clinical Oncology 15 (11):p3355-3362 Nov., 1997  
ISSN: 0732-183X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

4/3/8 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2003 Elsevier Science B.V. All rts. reserv.

11933828 EMBASE No: 2003044479  
T-cell costimulatory pathways relevant to transplant rejection and tolerance  
Wells A.D.  
Dr. A.D. Wells, Dept. of Pathology/Laboratory Med., Children's Hospital of Philadelphia, University of Pennsylvania, 3516 Civic Center Blvd., Philadelphia, PA 19104-4318 United States  
Transplantation Reviews ( TRANSPL. REV. ) (United States) 2002, 16/4 (205-219)  
ISSN: 0955-470X  
DOCUMENT TYPE: Journal ; Review  
LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 214

4/3/9 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2003 Elsevier Science B.V. All rts. reserv.

11449616 EMBASE No: 2002021386  
Expression of **CD40 ligand** (CD154) in B and T lymphocytes of  
Hodgkin disease: Potential therapeutic significance  
Clodi K.; Asgari Z.; Younes M.; Palmer J.L.; Cabanillas F.; Carbone A.;  
Andreeff M.; Younes A.  
Dr. A. Younes, Department of Lymphoma/Myeloma, University of Texas, M. D.  
Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030  
United States  
AUTHOR EMAIL: ayounes@notes.mdacc.tmc.edu  
Cancer ( CANCER ) (United States) 01 JAN 2002, 94/1 (1-5)  
CODEN: CANCA ISSN: 0008-543X  
DOCUMENT TYPE: Journal ; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 20

4/3/10 (Item 3 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2003 Elsevier Science B.V. All rts. reserv.

07928709 EMBASE No: 1999402580  
Constitutive expression and role of the TNF family ligands in apoptotic  
killing of tumor cells by human NK cells  
Kashii Y.; Giorda R.; Herberman R.B.; Whiteside T.L.; Vujanovic N.L.  
Dr. N.L. Vujanovic, University of Pittsburgh, Cancer Institute,  
Biomedical Science Tower W1045, 211 Lothrop Street, Pittsburgh, PA 15213  
United States  
AUTHOR EMAIL: vujanovicnl@msx.upmc.edu  
Journal of Immunology ( J. IMMUNOL. ) (United States) 15 NOV 1999,  
163/10 (5358-5366)  
CODEN: JOIMA ISSN: 0022-1767  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 37

4/3/11 (Item 4 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2003 Elsevier Science B.V. All rts. reserv.

07068504 EMBASE No: 1997350367  
**CD30** ligand in lymphoma patients with **CD30sup** + tumors  
Younes A.; Consoli U.; Snell V.; Clodi K.; Kliche K.-O.; Palmer J.L.;  
Gross H.J.; Armitage R.; Thomas E.K.; Cabanillas F.; Andreelf M.  
Dr. A. Younes, Department of Hematology, Section of Lymphoma, Texas M.D.  
Anderson Can. Ctr. Univ., 1515 Holcombe Blvd, Houston, TX 77030 United  
States  
AUTHOR EMAIL: ayounes@notes.mdacc.tmc.edu  
Journal of Clinical Oncology ( J. CLIN. ONCOL. ) (United States) 1997,  
15/11 (3355-3362)  
CODEN: JCOND ISSN: 0732-183X  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 24

4/3/12 (Item 1 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
(c) 2003 American Chemical Society. All rts. reserv.

138220374 CA: 138(15)220374h PATENT

Anti-CD3 and anti-T cell costimulatory molecule antibodies for producing human CD4+ Th1 cells for treating infection and cancer

INVENTOR(AUTHOR): Fowler, Daniel H.; Hou, Jeanne; Jung, Unsu; Gress, Ronald E.; Levine, Bruce; June, Carl

LOCATION: USA

ASSIGNEE: The Government of the United States of America as Represented by the Secretary of the Department of Health and Human Services; The Trustees of the University of Pennsylvania

PATENT: PCT International ; WO 200320904 A2 DATE: 20030313

APPLICATION: WO 2002US27824 (20020829) \*US PV316854 (20010831)

PAGES: 47 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

4/3/13 (Item 2 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

(c) 2003 American Chemical Society. All rts. reserv.

138088660 CA: 138(7)88660s PATENT

Monoclonal anti-CD3 antibodies for producing human CD4+ Th2 cells to treat graft versus host disease, tumors, and autoimmune disorders

INVENTOR(AUTHOR): Fowler, Daniel H.; Hou, Jeanne; Jung, Unsu; Gress, Ronald E.; Bishop, Michael; Levine, Bruce; June, Carl

LOCATION: USA

ASSIGNEE: United States of America, Health and Human Services; The Trustees of the University of Pennsylvania

PATENT: PCT International ; WO 200304625 A1 DATE: 20030116

APPLICATION: WO 2002US20415 (20020626) \*US PV302936 (20010702)

PAGES: 70 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-005/00A; C12N-005/02B; A61K-039/395B; C07K-016/00B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

4/3/14 (Item 3 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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137365329 CA: 137(25)365329m PATENT

Recombinant trimerizing fusion proteins and their use in disease treatment

INVENTOR(AUTHOR): Tschopp, Juerg; Schneider, Pascal

LOCATION: Switz.

ASSIGNEE: Apotech Research & Development Ltd.

PATENT: PCT International ; WO 200290553 A2 DATE: 20021114

APPLICATION: WO 2002EP5103 (20020508) \*DE 10122140 (20010508)

PAGES: 46 pp. CODEN: PIXXD2 LANGUAGE: German CLASS: C12N-015/62A; C07K-014/47B; C07K-014/525B; C07K-019/00B; C12N-001/21B; C12N-005/10B;

A61K-038/17B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

4/3/15 (Item 4 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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137088489 CA: 137(7)88489x PATENT  
Secreted Frizzled-related protein (sFRP) and protein motifs that interact with sFRP and therapeutic uses thereof  
INVENTOR(AUTHOR): Rubin, Jeffrey S.; Uren, Aykut; Horwood, Nicole Joy; Gillespie, Matthew Todd; Kay, Brian K.; Weisblum, Bernard  
LOCATION: USA  
ASSIGNEE: The Government of the United States of America, Department of Health and Human Services; St. Vincent's Institute of Medical Research  
PATENT: PCT International ; WO 200255547 A2 DATE: 20020718  
APPLICATION: WO 2002US869 (20020110) \*US PV260908 (20010110)  
PAGES: 81 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/00A; C07K-007/08B; C07K-007/06B; C12N-015/11B; A61K-038/04B; A61P-019/08B  
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

4/3/16 (Item 5 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
(c) 2003 American Chemical Society. All rts. reserv.

135348851 CA: 135(24)348851s PATENT  
Albumin fusion proteins with therapeutic proteins for improved shelf-life  
INVENTOR(AUTHOR): Rosen, Craig A.; Haseltine, William A.  
LOCATION: USA  
ASSIGNEE: Human Genome Sciences, Inc  
PATENT: PCT International ; WO 200179444 A2 DATE: 20011025  
APPLICATION: WO 2001US12013 (20010412) \*US PV229358 (20000412) \*US PV199384 (20000425) \*US PV256931 (20001221)  
PAGES: 606 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A  
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/17 (Item 6 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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135339226 CA: 135(24)339226q PATENT

Method for treatment of tumors using photodynamic therapy

INVENTOR(AUTHOR): Fanslow, William C., III; Thomas, Elaine K.

LOCATION: USA

ASSIGNEE: Immunex Corporation

PATENT: PCT International ; WO 200180888 A2 DATE: 20011101

APPLICATION: WO 2001US13616 (20010425) \*US PV199545 (20000425)

PAGES: 24 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/18 (Item 7 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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135104086 CA: 135(8)104086e PATENT

Multimerization domain-containing fusion proteins and use of fusion protein multimers for therapy and diagnosis

INVENTOR(AUTHOR): Tschopp, Juerg; Schneider, Pascal; Holler, Nils

LOCATION: Switz.

ASSIGNEE: Apotech Research and Development Ltd.

PATENT: PCT International ; WO 200149866 A1 DATE: 20010712

APPLICATION: WO 2000EP13032 (20001220) \*DE 19963859 (19991230)

PAGES: 96 pp. CODEN: PIXXD2 LANGUAGE: German CLASS: C12N-015/62A; C12N-015/11B; C07K-014/705B; A61K-038/17B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/19 (Item 8 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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134290751 CA: 134(21)290751v PATENT

Recombinant single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders

INVENTOR(AUTHOR): Halkier, Torben; Schambye, Hans Thalsgard; Okkels, Jens Sigurd; Andersen, Kim Vilbour; Nissen, Torben Lauesgaard; Soni, Bobby; Jeppesen, Claus Bekker; Van Den Hazel, Bart

LOCATION: Den.

ASSIGNEE: Maxygen Aps

PATENT: PCT International ; WO 200125277 A1 DATE: 20010412

APPLICATION: WO 2000DK563 (20001006) \*DK 991438 (19991007) \*DK 991855 (19991223) \*DK 20001119 (20000720)

PAGES: 123 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/525A; A61K-038/22B; A61P-029/00B; C07K-019/00B; C07K-001/107B; C12N-015/62B; C07K-014/52B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG;

SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/20 (Item 9 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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134290399 CA: 134(21)290399m PATENT  
Compositions and methods for tumor-targeted delivery of effector molecules  
INVENTOR(AUTHOR): Bermudes, David G.; King, Ivan C.; Clairmont, Caroline A.; Lin, Stanley L.; Belcourt, Michael  
LOCATION: USA  
ASSIGNEE: Vion Pharmaceuticals, Inc.  
PATENT: PCT International ; WO 200125397 A2 DATE: 20010412  
APPLICATION: WO 2000US23242 (20000824) \*US PV157500 (19991004) \*US PV157581 (19991004) \*US PV157637 (19991004)  
PAGES: 185 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A  
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/21 (Item 10 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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133191263 CA: 133(14)191263k JOURNAL  
Analysis of TNF-receptor and ligand superfamily molecules in patients with lymphoproliferative disease of granular lymphocytes  
AUTHOR(S): Zambello, Renato; Trentin, Livio; Facco, Monica; Siviero, Marta; Galvan, Silvia; Piazza, Francesco; Perin, Alessandra; Agostini, Carlo; Semenzato, Gianpietro  
LOCATION: Division of Hematology, Vicenza Hospital, Vicenza, Italy  
JOURNAL: Blood DATE: 2000 VOLUME: 96 NUMBER: 2 PAGES: 647-654  
CODEN: BLOOAW ISSN: 0006-4971 LANGUAGE: English PUBLISHER: American Society of Hematology

4/3/22 (Item 11 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
(c) 2003 American Chemical Society. All rts. reserv.

133163045 CA: 133(12)163045x PATENT  
Preparation of human effector T cells with CD86 on their surface and their therapeutic use  
INVENTOR(AUTHOR): Jeannin, Pascale; Delneste, Yves; Vittori, Marc; Bonnefoy, Jean-Yves  
LOCATION: Fr.  
ASSIGNEE: Pierre Fabre Medicament  
PATENT: PCT International ; WO 200046352 A1 DATE: 20000810  
APPLICATION: WO 2000FR240 (20000202) \*FR 991187 (19990202)  
PAGES: 55 pp. CODEN: PIXXD2 LANGUAGE: French CLASS: C12N-005/08A; A61P-037/00B; A61K-035/14B; C12N-005/10B; C07K-014/52B; A61K-039/00B; G01N-033/50B DESIGNATED COUNTRIES: AU; BR; CA; CN; JP; MX; US; ZA  
DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT;

LU; MC; NL; PT; SE

4/3/23 (Item 12 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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133145450 CA: 133(11)145450w PATENT  
M68: a soluble member of the tumor necrosis factor receptor family  
identified by gene discovery and its uses  
INVENTOR(AUTHOR): Bai, Chang  
LOCATION: USA  
ASSIGNEE: Merck and Co., Inc.  
PATENT: PCT International ; WO 200046247 A1 DATE: 20000810  
APPLICATION: WO 2000US3037 (20000204) \*US PV118902 (19990205) \*US  
PV172754 (19991220)  
PAGES: 86 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/47A;  
C07H-021/04B; C12N-015/62B; C12N-015/63B; C12N-005/22B; G01N-033/52B;  
G01N-033/53B; A61K-031/70B; A61K-038/17B DESIGNATED COUNTRIES: CA; JP; US  
DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT;  
LU; MC; NL; PT; SE

4/3/24 (Item 13 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
(c) 2003 American Chemical Society. All rts. reserv.

129329705 CA: 129(25)329705g PATENT  
Receptor protein and its use  
INVENTOR(AUTHOR): Nishi, Kazunori; Shintani, Atsushi; Horiguchi, Takashi  
LOCATION: Japan,  
ASSIGNEE: Takeda Chemical Industries, Ltd.  
PATENT: European Pat. Appl. ; EP 873998 A2 DATE: 19981028  
APPLICATION: EP 98303190 (19980424) \*JP 97109798 (19970425) \*JP 97251867  
(19970917)  
PAGES: 65 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C07K-014/705A;  
C07K-016/28B; C12N-015/12B DESIGNATED COUNTRIES: AT; BE; CH; DE; DK; ES;  
FR; GB; GR; IT; LI; LU; NL; SE; MC; PT; IE; SI; LT; LV; FI; RO

4/3/25 (Item 14 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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129077575 CA: 129(7)77575f PATENT  
Novel expression vectors containing accessory molecule ligand genes and  
their use for immunomodulation and treatment of malignancies and autoimmune  
disease  
INVENTOR(AUTHOR): Kipps, Thomas J.; Sharma, Sanjai; Cantwell, Mark  
LOCATION: USA  
ASSIGNEE: University of California  
PATENT: PCT International ; WO 9826061 A2 DATE: 19980618  
APPLICATION: WO 97US22740 (19971208) \*US 32145 (19961209) \*US 982272  
(19971201)  
PAGES: 167 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/00A;  
A61K-048/00B DESIGNATED COUNTRIES: AT; AU; BR; CA; CH; CN; DE; DK; ES; FI;  
GB; IL; JP; KR; LU; MX; NO; NZ; PT; RU; SE; SG DESIGNATED REGIONAL: AT; BE  
; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE  
? t s4/7/1-10

4/7/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13501169 BIOSIS NO.: 200200129990

Depletion of normal B-lymphocytes by rituximab therapy alters serum cytokine levels, resolves B-symptoms and induces clinical remissions in patients with relapsed classical Hodgkin's disease (HD).

AUTHOR: Younes Anas(a); Romaguera Jorge(a); Hagemeister Frederick(a); McLaughlin Peter(a); Rodriguez Maria Alma(a); Fiumara Paolo(a); Goy Andre(a); Jeha Sima; Manning John; Medeiros L Jeffrey; Martinez Rudy F(a); Cabanillas Fernando(a)

AUTHOR ADDRESS: (a)Lymphoma/Myeloma, M.D.Anderson Cancer Center (MDACC), Houston, TX\*\*USA

JOURNAL: Blood 98 (11 Part 1):p132a November 16, 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001

ISSN: 0006-4971

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Although the malignant Hodgkin and Reed-Sternberg (H/RS) cells of HD are predominantly of B cell origin, only in 25%-30% of the cases they express CD20 antigen. However, infiltrating benign CD20-positive B cells in HD lymph nodes frequently express **CD30** ligand and **CD40** ligand that can provide H/RS cells with survival signals, suggesting that B-cells of HD may play a role in the growth regulation of H/RS cells in vivo. With this background, we hypothesized that depletion of the CD20-positive normal B cells from HD lesions may deprive the H/RS cells from important survival factors and could lead to clinical responses. To test this hypothesis, we initiated a pilot study of single agent rituximab for the **treatment** of patients with relapsed classical HD. All patients received 6 weekly doses of 375 mg/m<sup>2</sup> rituximab. **Tumor** response was determined at week 9 and every 3 months thereafter. Twenty-four patients were enrolled, of whom 22 patients are evaluable for treatment response. All patients had nodular sclerosis histology. Median number of prior treatment regimens was 4 (range 2 to 12), and 18 patients had prior bone marrow or stem cell transplantation. Relapses involved extranodal sites in 12 patients. CD20 expression on H/RS was observed in 5 cases. Five (23%) patients achieved partial or complete remissions (2 expressed CD20 on H/RS cells), and 8 (36%) had stable disease. All responses were seen in patients whose disease did not involve extranodal sites and were irrespective of CD20 expression on H/RS cells. Seven patients had B symptoms prior to rituximab therapy, which resolved in 6 after therapy (3 had also had clinical responses). Serum levels of IL-6, IL-10, IL-12, IL-13, and interferon-gamma were measured in 8 patients before and after rituximab therapy by ELISA. Rituximab therapy significantly decreased IL-6 levels in 2 patients who also achieved partial remissions. IL-10 levels decreased in 3 patients but did not correlate with clinical responses. None of the patients had detectable levels of serum IL-12, interferon-gamma, or IL-13. Our data suggest that depletion of normal B cells in patients with relapsed classical HD can alter cytokine levels, improve B-symptoms, and may result in clinical remissions especially in patients whose disease is limited to the lymph nodes. Based on these data we are currently combining rituximab with chemotherapy for the treatment of patients with classical HD to explore whether depletion of normal B cells from HD lesions may enhance the activity of chemotherapy.

4/7/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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13112983 BIOSIS NO.: 200100320132

A pilot study of rituximab in patients with relapsed Hodgkin's disease of classical type.

AUTHOR: Younes A(a); Romaguera J(a); Hagemeister F(a); Rodriguez M(a);  
McLaughlin P(a); Medeiros J(a); Cabanillas F(a)  
AUTHOR ADDRESS: (a)U.T. M.D. Anderson Cancer Center, Houston, TX\*\*USA  
JOURNAL: Blood 96 (11 Part 1):p733a November 16, 2000  
MEDIUM: print

CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of  
Hematology San Francisco, California, USA December 01-05, 2000

SPONSOR: American Society of Hematology

ISSN: 0006-4971

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: We have previously reported that normal B lymphocytes in lymph nodes and peripheral blood of patients with Hodgkin's disease (HD) express **CD40 Ligand (CD40L)** and **CD30 Ligand (CD30L)**. Both ligands can activate NF-kappabeta and promote Reed-Sternberg (RS) cell survival. Therefore, we hypothesized that elimination of B lymphocytes from HD lesions may deprive the RS cells of important growth signals and may result in **tumor** regression. To examine this hypothesis, we **treated** patients with relapsed classic HD with 375 mg/m2 of rituximab IV every week for 6 consecutive weeks. Patients were eligible if they had relapsed classic HD, regardless of CD20 antigen expression on RS cells, and had at least two prior treatment regimens. Patients were excluded if they were pregnant women, had lymphocyte depletion or lymphocyte-predominant histology, were infected with HIV virus, or had CNS involvement by lymphoma. Objective tumor response was assessed after completion of six doses. Eighteen patients with nodular sclerosis histology are enrolled, of whom 15 have completed the planned therapy and are evaluable for response. CD20 antigen was expressed by the RS cells in 5 patients. Patient age ranged between 17 and 66 years and the number of prior treatment regimens ranged between 2 and 7 (median, 5 regimens). Thirteen patients had prior bone marrow transplantation. Seven patients had disease limited to lymph nodes and 8 had disease involving lymph nodes plus lungs and/or liver. Three patients (20%) had major responses (2 PRs and 1 CRu). All responding patients had disease limited to lymph nodes and the RS cells did not express CD20. Six additional patients had stable disease of whom 2 experienced resolution of B symptoms. We conclude that rituximab therapy, possibly by eliminating normal B lymphocytes from HD patients, can result in major clinical responses and symptom improvement.

4/7/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13057538 BIOSIS NO.: 200100264687  
Chronic lymphocytic leukemia B cells impair immunoglobulin class switching by inducing **CD30+** suppressor T cells.

AUTHOR: Cerutti Andrea(a); Kim Edmund C(a); Zan Hong(a); Schaffer Andras(a); Casali Paolo(a)

AUTHOR ADDRESS: (a)Weill Medical College of Cornell University, 1300 York Avenue, New York, NY, 10021\*\*USA

JOURNAL: FASEB Journal 15 (5):pA1202 March 8, 2001

MEDIUM: print

CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001

ISSN: 0892-6638

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** B cell chronic lymphocytic leukemia (CLL) is a chronic lymphoproliferative disorder associated with impaired Ig class switching from IgM to IgG and IgA, a defect that leads to recurrent infections. The pathogenesis of this immunodeficiency is poorly understood. Naive B cells undergo class switching upon engagement of CD40 by CD154 (**CD40 ligand**), a molecule expressed by T cells a few hours after activation by antigen. Four days later, T cells express **CD30**, a negative modulator of the immune response. We show here that leukemic CLL B cells rapidly up-regulate T cell **CD30** through a CD134 ligand (OX40 ligand) and IL-4-dependent mechanism. These **CD30+** T cells **inhibit** class switch DNA recombination by engaging CD153 (**CD30 ligand**), a molecule that interferes with the assembly of the CD40: **tumor** necrosis factor receptor associated factor (TRAF) complex in CD154-activated naive B cells. By showing that engagement of T cell **CD30** by CD153 on leukemic B cells down-regulates CD154, our findings suggest that, in CLL, dysregulated **CD30:CD153** interaction impairs class switching by transmitting bidirectional CD40 and CD154-inhibitory signals.

4/7/4 (Item 4 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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13033028 BIOSIS NO.: 200100240177  
Thiols decrease cytokine levels and down-regulate the expression of **CD30** on human allergen-specific T helper (Th) 0 and Th2 cells.  
AUTHOR: Bengtsson A(a); Lundberg M; Avila-Carino J; Jacobsson G; Holmgren A; Scheynius A  
AUTHOR ADDRESS: (a) Department of Medicine, Unit of Clinical Allergy Research, Karolinska Hospital L2: 04, 171 76, Stockholm: asa.bengtsson@mb.ks.se\*\*Sweden  
JOURNAL: Clinical and Experimental Immunology 123 (3):p350-360 March, 2001  
MEDIUM: print  
ISSN: 0009-9104  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

**ABSTRACT:** The thiol antioxidant N-acetyl-L-cysteine (NAC), known as a precursor of glutathione (GSH), is used in AIDS **treatment** trials, as a chemoprotectant in **cancer** chemotherapy and in **treatment** of chronic bronchitis. In vitro, GSH and NAC are known to enhance T cell proliferation, production of IL-2 and up-regulation of the IL-2 receptor. The 120-kD **CD30** surface antigen belongs to the tumour necrosis factor (TNF) receptor superfamily. It is expressed by activated T helper (Th) cells and its expression is sustained in Th2 cells. We have analysed the effect of GSH and NAC on the cytokine profile and **CD30** expression on human allergen-specific T cell clones (TCC). TCC were stimulated with anti-CD3 antibodies in the presence of different concentrations of GSH and NAC. Both thiols caused a dose dependent down-regulation of IL-4, IL-5 and IFN-gamma levels in Th0 and Th2 clones, with the most pronounced decrease of IL-4. Furthermore, they down-regulated the surface expression of **CD30**, and the levels of soluble **CD30** (sCD30) in the culture supernatants were decreased. In contrast, the surface expression of CD28 or **CD40 ligand** (**CD40L**) was not significantly changed after treatment with 20 mM NAC. These results indicate that GSH and NAC favour a Th1 response by a preferential down-regulation of IL-4. In addition, the expression of **CD30** was down regulated by GSH and NAC, suggesting that **CD30** expression is dependent on IL-4, or modified by NAC. In the likely event that **CD30** and its soluble counterpart prove to contribute to the pathogenesis in Th2 related diseases such as allergy, NAC may be

considered as a future therapeutic agent in the treatment of these diseases.

4/7/5 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12615531 BIOSIS NO.: 200000369033

TTRAP, a novel protein that associates with CD40, **tumor** necrosis factor (TNF) receptor-75 and TNF receptor-associated factors (TRAFs), and that **inhibits** nuclear factor-kappaB activation.

AUTHOR: Pype Stefan; Declercq Wim; Ibrahimi Abdelilah; Michiels Christine; Van Rietschoten Johanna G I; Dewulf Nathalie; de Boer Mark; Vandenabeele Peter; Huylebroeck Danny(a); Remacle Jacques E

AUTHOR ADDRESS: (a)Department of Cell Growth, Differentiation and Development, Flanders Interuniversity Institute for Biotechnology, University of Leuven, Herestraat 49, Campus Gasthuisberg, B-3000, Leuven  
\*\*Belgium

JOURNAL: Journal of Biological Chemistry 275 (24):p18586-18593 June 16, 2000

MEDIUM: print

ISSN: 0021-9258

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: CD40 belongs to the tumor necrosis factor (TNF) receptor family. CD40 signaling involves the recruitment of TNF receptor-associated factors (TRAFs) to its cytoplasmic domain. We have identified a novel intracellular CD40-binding protein termed TRAF and TNF receptor-associated protein (TTRAP) that also interacts with TNF-R75 and **CD30**. The region of the CD40 cytoplasmic domain that is required for TTRAP association overlaps with the TRAF6 recognition motif. Association of TTRAP with CD40 increases profoundly in response to treatment of cells with **CD40L**. Interestingly, TTRAP also associates with TRAFs, with the highest affinity for TRAF6. In transfected cells, TTRAP inhibits in a dose- dependent manner the transcriptional activation of a nuclear factor-kappaB (NF-kappaB)-dependent reporter mediated by CD40, TNF-R75 or Phorbol 12-myristate 13-acetate (PMA) and to a lesser extent by TRAF2, TRAF6, TNF-alpha, or interleukin-1beta (IL-1beta). TTRAP does not affect stimulation of NF-kappaB induced by overexpression of the NF-kappaB-inducing kinase (NIK), the IkappaB kinase alpha (IKKalpha), or the NF-kappaB subunit P65/RelA, suggesting it acts upstream of the latter proteins. Our results indicate that we have isolated a novel regulatory factor that is involved in signal transduction by distinct members of the TNF receptor family.

4/7/6 (Item 6 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11525042 BIOSIS NO.: 199800306374

Enhancement of antitumor immunity by expression of CD70 (CD27 ligand) or CD154 (**CD40 ligand**) costimulatory molecules in tumor cells.

AUTHOR: Couderc Bettina; Zitvogel Laurence; Douin-Echinard Victorine; Djennane Leila; Tahara Hideaki; Favre Gilles; Lotze Michael T; Robbins Paul D(a)

AUTHOR ADDRESS: (a)Dep. Mol. Genet. and Biochem., W1246 Biomed. Sci. Tower, Univ. Pittsburgh Sch. Med., Pittsburgh,\*\*USA

JOURNAL: Cancer Gene Therapy 5 (3):p163-175 May-June, 1998

ISSN: 0929-1903

DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: CD70 (CD27 ligand (CD27L)), CD153 (**CD30L**), and CD154 (**CD40L**) are members of the tumor necrosis factor family of costimulatory molecules and expressed on the surface of T cells that are important for both T- and B-cell help. We examined the capacity for expression of these tumor necrosis factor family members on tumor cells to induce an antitumor response either in the presence or absence of interleukin 12. Retroviral vectors were constructed that expressed high levels of membrane bound CD70, CD153, or CD154 following infection and selection of the murine tumor lines MCA 207 or TS/A. The genetically modified tumor cells expressing these molecules were able to stimulate splenic cell proliferation, demonstrating that the expressed costimulatory molecules were biologically active. When tested for tumor establishment, the expression of either CD70 or CD154 was able to slow **tumor** growth. Similarly, CD70 or CD154 were able to induce antitumor immunity at a higher frequency when tested in **vaccination and therapy** models. CD70 was able to induce antitumor immunity at a level similar to CD80 when tested either in the presence or absence of interleukin 12. Moreover, coexpression of CD70 and CD80 was able to synergize the induction of a higher frequency of antitumor immunity in a vaccination model. Taken together, our results suggest that CD154 and in particular CD70 are able to contribute to the induction of the immune response to tumor in murine models and thus may be of use for human clinical trials.

4/7/7 (Item 7 from file: 5)  
DIALOG(R)File 5:BIOSIS Previews(R)  
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11226541 BIOSIS NO.: 199800007873  
**CD30** ligand in lymphoma patients with **CD30!**+ tumors.  
AUTHOR: Younes Anas(a); Consoli Ugo; Snell Virginia; Clodi Katharina; Kliche Kay-Oliver; Palmer J Lynn; Gruss Hans J; Armitage Richard; Thomas Elaine K; Cabanillas Fernando; Andreeff Michael  
AUTHOR ADDRESS: (a)Dep. Hematol., Section Lymphoma, Univ. Texas M.D. Anderson Cancer Cent., 1515 Holcombe Blvd., Ho\*\*USA  
JOURNAL: Journal of Clinical Oncology 15 (11):p3355-3362 Nov., 1997  
ISSN: 0732-183X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Purpose: **CD30** ligand (**CD30L**), which is expressed on resting B and activated T lymphocytes, can induce cell death in several **CD30!**+ cell lines. Patients with **CD30!**+ tumors (Hodgkin's disease and Ki-1!+ non-Hodgkin's lymphoma) frequently have elevated soluble **CD30** (sCD30) levels in their serum, which correlates with a poor prognosis. The role of sCD30 in protecting tumor cells from **CD30L**-mediated cell death and the pattern of **CD30L** expression on human peripheral-blood lymphocytes (PBLs) of normal donors and patients with **CD30!**+ tumors are investigated. Materials and Methods: **CD30L** surface protein expression was determined by two-color flow cytometry on PBLs of patients with **CD30!**+ tumors and normal individuals. **CD30L** levels were determined on subsets of PBLs before and after stimulation with phytohemagglutinin (PHA), anti-CD3 antibody, or **CD40L**. sCD30 was measured by enzyme-linked immunosorbent assay (ELISA). The apoptotic activity of membrane-bound **CD30L** was tested in a **CD30!**+ cell line by the annexin V-binding method. Results: Unstimulated T lymphocytes of normal donors and patients with lymphoma rarely expressed **CD30L** surface protein,



but were able to express it after stimulation with PHA or anti-CD3 antibody. Resting B cells of patients with **CD30!+** tumors had lower levels of detectable surface **CD30L** compared with normal donors (mean, 55% and 80.6%, respectively;  $P = .0008$ ). Patients with high levels of serum sCD30 had lower detectable levels of **CD30L** on their PBLs ( $R!2 = .72$ ,  $P = .0008$ ) and exogenous sCD30 **blocked** membrane-bound **CD30L**-mediated apoptosis in a **CD30!+** cell line. Conclusion: In patients with **CD30!+ tumors**, sCD30 can decrease the availability of **CD30L** on PBLs. **Blocking** the apoptosis-inducing activity of **CD30L** by its soluble receptor may explain how **CD30!+ tumors** escape immunosurveillance and may be related to the reported poor prognosis of patients who have elevated sCD30 levels.

4/7/8 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
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11933828 EMBASE No: 2003044479  
T-cell costimulatory pathways relevant to transplant rejection and tolerance  
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Transplantation Reviews ( TRANSPL. REV. ) (United States) 2002, 16/4 (205-219)  
ISSN: 0955-470X  
DOCUMENT TYPE: Journal ; Review  
LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 214

4/7/9 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
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11449616 EMBASE No: 2002021386  
Expression of **CD40 ligand** (CD154) in B and T lymphocytes of Hodgkin disease: Potential therapeutic significance  
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Cancer ( CANCER ) (United States) 01 JAN 2002, 94/1 (1-5)  
CODEN: CANCA ISSN: 0008-543X  
DOCUMENT TYPE: Journal ; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 20

BACKGROUND. The malignant Hodgkin and Reed-Sternberg (H/RS) cells of Hodgkin disease (HD) express **CD30** and **CD40** receptors that can activate nuclear factor kappa B and transduce survival signals. The authors have reported previously that the B lymphocytes of HD express **CD30** ligand (**CD30L**, CD153). Furthermore, they and others have reported previously that the **CD40L** survival pathway is augmented in patients with B-cell malignancies, as **CD40L** was constitutively expressed by the malignant B cells and infiltrating T cells, and sera from those patients contained elevated levels of soluble **CD40L**. In this study, the authors investigated the hypothesis that the survival of H/RS cells was similarly promoted by an augmented **CD40L** signals in HD patients.

METHODS. The expression of **CD40L** on lymphocyte subsets of patients with classic HD was determined by two-color fluorescent-activated cell sorter analysis. Serum soluble **CD40L** levels were determined by enzyme linked immunosorbent assay. RESULTS. **CD40L** was constitutively expressed on both the T and B cells of HD patients but was more prominently expressed on the B lymphocytes. Soluble **CD40L** was detected in the serum of 17 of 37 patients (45%) and was higher than 1 ng/mL in 4 patients (10%). Both interleukin (IL)-4 and IL-10, which are known to be secreted by H/RS cells and surrounding T cells, up-regulated **CD40L** expression on normal B cells. CONCLUSIONS. Thus, the expression of **CD40L** and **CD30L** on the B cells of HD patients suggests that B lymphocytes may play a role in the regulation of H/RS cell growth in vivo. Depriving H/RS cells from **CD30L** and **CD40L** survival signals by eliminating B cells from HD lesions may be of **therapeutic** value. (c) 2002 American Cancer Society.

4/7/10 (Item 3 from file: 73)  
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07928709 EMBASE No: 1999402580  
 Constitutive expression and role of the TNF family ligands in apoptotic killing of tumor cells by human NK cells  
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 Journal of Immunology ( J. IMMUNOL. ) (United States) 15 NOV 1999,  
 163/10 (5358-5366)  
 CODEN: JOIMA ISSN: 0022-1767  
 DOCUMENT TYPE: Journal; Article  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
 NUMBER OF REFERENCES: 37

Natural killer cells mediate spontaneously secretory/necrotic killing against rare leukemia cell lines and a nonsecretory/apoptotic killing against a large variety of tumor cell lines. The molecules involved in nonsecretory/apoptotic killing are largely undefined. In the present study, freshly isolated, nonactivated, human NK cells were shown to express TNF, lymphotoxin (LT)-alpha, LT-beta, Fas ligand (L), CD27L, **CD30L**, OX40L, 4-1BBL, and TNF-related apoptosis-inducing ligand (TRAIL), but not **CD40L** or nerve growth factor. Complementary receptors were demonstrated to be expressed on the cell surface of solid tumor cell lines susceptible to apoptotic killing mediated by NK cells. Individually applied, antagonists of TNF, LT-alpha, FasL, or FasL fully **inhibited** NK cell-mediated apoptotic killing of **tumor** cells. On the other hand, recombinant TNF, LT-alpha, FasL, or FasL applied individually or as pairs were not cytotoxic. In contrast, a mixture of the three ligands mediated significant apoptosis in tumor cells. These findings demonstrate that human NK cells constitutively express several of the TNF family ligands and induce apoptosis in tumor cells by simultaneous engagement of at least three of these cytotoxic molecules.

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Set	Items	Description
S1	745	(CD40L OR CD40(W)LIGAND) AND (TREAT? OR THERAP? OR PREVENT? OR SUPPRESS? OR BLOCK? OR INHIBIT?) (20N) (CANCER? OR TUMOR? OR TUMOUR?)
S2	1	S1 AND PHOTODYNAMIC
S3	33	S1 AND CD30?

S4  
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25 RD S3 (unique items)